result in misdiagnosis and almost certainly will result in reduced immunotherapeutic efficacy.

Although a number of methods are potentially useful, those with the most promise for standardization include specific antigen analysis and radioallergosorbent test (RAST) inhibition. Isoelectric focusing, although not quantitative, is a simple physicochemical procedure that provides a graphic demonstration of the quality and identity of an extract and is especially valuable with pollen extracts. The in vitro methods derived from quantitative skin testing have been shown to correlate with a relative potency.

Currently, extracts of venoms of stinging insects are standardized as well as extracts of short-ragweed pollen. Before 1983 a number of other standardized extracts should become available, including extracts for use in pollen and cat allergy. The standardized extracts will not only improve the practice of allergy but will aid investigations into fundamental aspects of allergic disease.

Standardized extracts should permit interchangeability of extracts from one manufacturer to another. In some instances, these extracts may be more potent or reactive than currently available extracts and may have an earlier expiration date, especially for high dilutions.

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Immunologic Benefits of Breast Feeding

RESULTS OF NUMEROUS clinical and laboratory studies leave little doubt that human milk is best for infants and especially so in families with allergies. Colostrum provides a neonate with a concentrated dose of antibodies, stimulates the passage of meconium and thereby the excretion of bilirubin, and helps establish nonpathogenic *Lactobacillus bifidus* as a predominant organism of the gastrointestinal flora.

Mature breast milk is the ideal nutrient during infancy. A predominance of whey protein results in a soft, digestible curd. The amino acid content is especially appropriate for rapid growth. Lipid digestion and absorption, facilitated by the presence of lipases, is nearly complete. Minerals such as iron are more bioavailable. The renal solute load is low, providing a substantial margin of safety while kidney function is maturing.

The continuing presence of immunoglobulins, a number of nonspecific antiinfective factors including lysozyme, lactoferrin, interferon, complement and the bifidus factor, as well as viable cellular components, offer an important passive protection against enteric and respiratory pathogens. Additionally, penetration of the immature gastrointestinal mucosal barrier by potentially allergenic antigens is inhibited by substances in breast milk.

Bonding and healthy psychological development are naturally promoted by the frequent physical contact and reciprocal neuroendocrine interaction between a nursing mother and infant. There are neuroendocrine reflexes that are also beneficial to maternal health. Oxytocin, responsible for the milk-ejection reflex, stimulates uterine contractions, which decrease postpartum bleeding and facilitate uterine involution. Elevated prolactin levels delay the return of ovulation and menstruation.

Because of the many benefits, breast-feeding should be actively encouraged among expectant parents. Ideally nursing should continue for as much of the first year of life as possible, with gradual introduction of solid foods after the fifth or sixth month. For families with allergies, exclusive breast-feeding with attention to the nursing mother's diet appears to delay or prevent allergic diseases in offspring.

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Monoclonal Antibodies

IN 1975 Milstein and Köhler, while studying the genetic regulation of antibody synthesis in mice, described a technique of fusing together normal antibody-producing cells and myeloma cells. Some of the resulting hybrid cells acquired two highly desirable characteristics: continuous replication typical of the myeloma cell and synthesis of antibody specified by the normal B cell. These fused cells can be grown as clones of a

single cell, and the resulting clone is termed a hybridoma. Hybridomas may be maintained in Petri dishes and antibody harvested from the supernatant. Alternatively they can be reinserted into the peritoneal cavity of a mouse and the antibody-rich peritoneal fluid withdrawn. Both methods can produce monospecific antibody in relatively large amounts.

Monoclonal antibodies have already had a major impact on biomedical research and are beginning to improve both laboratory and clinical medicine. In vitro diagnostic assays in which polyclonal antibodies have been used in the past, for example, radioimmunoassay and enzyme immunoassay, are more and more incorporating monoclonal technology. The first kit using a monoclonal antibody approved by the Food and Drug Administration was for a radioimmunoassay to measure serum IgE. Other kits will be available soon, including one using a monoclonal antibody to measure serum theophylline concentrations. A higher degree of quality control will exist because a permanent source of a monospecific antibody reagent is now possible. Monoclonal antibodies are also being developed against drugs, hormones, microbial antigens and proteins and will soon become part of routine hospital diagnostic repertoires.

Monoclonal antibodies specific for tumor antigens conjugated with short-lived radionuclides are being developed for in vivo cancer detection. Such an antitumor antibody by itself or conjugated to chemotherapeutic agents has proved useful in treating cancer in laboratory animals and phase I and II trials in humans are underway. A monoclonal antibody for the cytotoxic lymphocyte that causes renal graft rejection has been used to stop rejection episodes.

Because antibodies can be developed that eliminate lymphocytes responsible for graft versus host disease, transplantation across histocompatibility barriers may be possible. Removal of these cells from bone marrow, and transplantation of the depleted marrow elements into lethally irradiated cancer patients is being investigated for the treatment of otherwise fatal leukemias. In drug overdose (for example, theophylline, digoxin) these antibodies can be used to rapidly reduce toxic serum concentrations. There is no field of medicine, either in vivo or in vitro diagnostics, or in vivo therapeutics, that will not be affected by monoclonal antibody technology.

Potential allergic reactions to murine monoclonal antibodies must be kept in mind because the administration of foreign protein can cause both serum sickness reactions and IgE sensitization. Radioallergosorbent test (RAST) for IgE antimurine protein is not available, but skin testing with the relevant monoclonal antibody should point to IgE-mediated reactions.

In fewer than seven years the technique of cell fusion has been developed for practical application. All physicians will need to be knowledgeable about this exciting advance in the evaluation and care of patients.

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Immunoglobulin Subclass IgG4 Deficiency

ELECTROPHORETICALLY fast-moving IgG homocytotropic antibodies are known to play a role in local anaphylactic reactions in rodents and have been suspected of being important in human hypersensitivity reactions. Antibodies of the subclass IgG4 are the most likely candidates in humans. The development of a radioimmunoassay specific for IgG4 has made it possible to measure IgG4 levels in humans of all ages. A number of persons have been found with definitely elevated levels of IgG4 (above 1,000 μg per ml, or 100 mg per dl). Nearly all of these have proved to be highly allergic people and some have had high levels of antigen-specific IgG4 antibodies but no increase in total or antigen-specific IgE.

In one report four persons who had an apparent absence of IgG4 (serum levels below 1 μg per ml) were discussed. Since that initial report eight more persons have been found with profound deficiency of serum IgG4. Eleven of these patients have had a syndrome of severe recurrent infections of sinuses, middle ear and lungs. Recurring pneumonia, often associated with bronchiectasis, constitutes the most ominous finding. We estimate that in 20 percent to 25 percent of persons with "idiopathic" bronchiectasis there is an isolated deficiency of IgG4.

In addition, persons with IgA deficiency or common variable immunodeficiency with recurrent pneumonia, bronchiectasis (or both) frequently have an absence of detectable IgG4,